of Malaria Deaths in Rural Burkina Faso

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Malaria is the leading cause of death among children less than 5 years in sub-Saharan Africa, however, precise estimates on the burden of malaria are lacking. The aim of this study was to describe temporal trends for malaria and all-cause mortality, by combining a series of clinical and intervention studies conducted in a rural setting in Burkina Faso. A meta-analysis of original study data was conducted, with children under five years who participated in five observational and intervention studies between June 1999 and December 2004 in rural North-western Burkina Faso. Data collected by the Demographic Surveillance System (DSS) in the Nouna research zone was used for monitoring mortality (ascertained from the verbal autopsy questionnaire). Person-years (PY) of observations were computed and age-standardized mortality rates for all-causes and malaria (adjusted for missing causes of death) were calculated. Rate ratios to investigate mortality variations over years were calculated using multivariate Poisson regression. The study sample contained 6387 children aged less than 5 years (mean follow-up: 2.8 years; 16099 PY). During the study period, 443 deaths were recorded with malaria accounting for 46% of all deaths. The all-cause and malaria specific mortality rates were 26.7 (95% CI: 24.2—29.2) and 16.0 (95% CI: 14.3—17.8) per 1,000 PY. All-cause mortality rates declined over years of follow-up (from 28.0 to 16.3 per 1,000 PY in 2000 to 2004 respectively) but malaria mortality rates remained rather stable (from 13.0 to 11.0 per 1,000 PY in 2000 to 2004 respectively) resulting in an increasing relative effect of malaria on all-cause mortality. Variations in all-cause and malaria-specific mortality were observed with increasing age and across village clusters. The findings of this study support the continuously decreasing trend of all cause mortality in most of SSA but call for more efforts to comprehensively address malaria with existing control tools such as insecticide-treated bed nets and effective first-line combination therapies.

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48.001

Evaluation T-Spot TB Test in Diagnosis Tuberculosis

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Introduction: Tuberculosis (TB) is a chronic infection disease. More than half of the untreated patients will die during the period of five years after diagnosis. The main goal in TB program is early diagnosis and treatment. Some biochemical tests such as T-SPOT serology could be useful for the rapid diagnosis of tuberculosis.

Materials and Methods: We conducted a cross-sectional study in 60 patients with TB. 30 patients were sputum positive and the remainder were sputum negative for acid fast bacilli

Results: 23 out of 30 patients with sputum positive TB were T SPOT serology positive and 12 out of 30 patients with sputum negative TB were serology positive. The sensitivity/specificity/positive predictive value/negative predictive value/Like Hood Ratio were 76%/40%/56%/63%/1/25 respectively.

Discussion: In summary by using this test we could not differentiate between active and latent infection. Despite the high risk of infection of tuberculosis in this region, the increased pulmonary infection other than TB and lower like hood ratio this test would not help as a valuable diagnostic method.

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Comparison of IFN-Gamma Assay and Tuberculin Skin Test for Detecting Latent Tuberculosis Infection in BCG-Vaccinated Population

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Objective: Screening for latent tuberculosis infection (LTBI) with Mantoux tuberculin skin test (TST) has many limitations. Some studies showed that IFN-gamma assay is a better indicator of the risk of M tuberculosis infection than TST in a BCG-vaccinated subjects. In this study we aimed to compare the IFN-gamma assay with the TST for detecting LTBI in BCG-vaccinated population.

Patients and Methods: 186 BCG-vaccinated subjects enrolled in study. They underwent TST and IFN-gamma assay. They divided in two groups. Group 1 includes individuals who were at low risk for exposure to M. tuberculosis (LRG) and

Group 2 includes individuals who were likely to have been exposed to M. tuberculosis infections (HRG).

Results: Overall agreement between IFN-gamma assay and TST was 89.3% (kappa = 0.052). In LRG, agreement between the two tests was 52.6% (95% confidence interval, 44—60%) with κ values of 0.019. In HRG agreement between the two tests was 63.2% (95% confidence interval, 42—84%) with κ values of 0.28.

Conclusion: In conclusion, the IFN-gamma assay showed acceptable results for determining latent M. tuberculosis infection in vaccinated population. Although TST and IFN-gamma assay appear comparable, they have different performance and operational characteristics; therefore, the decision to select one test over the other will depend on the population, purpose of testing, and resource availability.

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48.003

Real-Time PCR for the Detection of Fluoroquinolone Resistance in *Mycobacterium Tuberculosis*

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Background: A Fluoroquinolone (FQN) is the drug of first choice for the treatment of multi-drug resistant tuberculosis (MDR TB) but the FQN-resistance rate in Vietnam is unknown. A rapid and effective test to detect FQN-resistance before treatment is urgently needed. FQNs inhibit the function of the DNA gyrase, encoded by the *gyrAB* genes of *Mycobacterium tuberculosis* and mutations in the Quinolone Resistance Determining Region (QRDR) of *gyrA* have been shown to account for 60—70% of FQN-resistant isolates. A Real-time-PCR (RT-PCR) test was developed to detect the most common mutations in this region.

Methods: gyrA sequencing data from 40 FQN-sensitive and 42 FQN-resistant (ofloxacin 2 μg/ml) clinical isolates was used to develop the RT-PCR test. Three Locked-Nucleic-Acid probes were used to detect mutations at codons 90, 91 or 94 which accounted for 97% of the FQN-related mutations in QRDR of *gyrA*. A set of 131 consecutive isolates from retreatment patients from Pham Ngoc Thach Hospital, resistant to either Isoniazid or Rifampin, was used to evaluate the RT-PCR and estimate the resistance rate.

Results: Sequencing data showed that all 40 FQN-sensitive isolates were wild-type in the QRDR. Among 42 FQN-resistant isolates, 10 were wild-type, 20 carried single mutations and, surprisingly, 12 were heterogeneous containing both wild-type and mutated populations. Of these 12, 4 contained a mutation at 2 resistance-associated alleles. The RT-PCR test identified all wild-type and single mutation isolates correctly and 12/16 mutations in heterogeneous isolates. Five percent of isolates (7/131) from retreatment patients were identified as FQN-resistant by RT-PCR and confirmed by sequencing.

Conclusion: This RT PCR assay is a quick, relatively simple and cheap test to screen for FQN-resistance with 100% specificity. FQN resistance is estimated at > 5% in retreatment patients in Southern Vietnam. Studies to determine other FQN-resistance mechanisms are vital to improve molecular diagnosis and treatment.

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48.004

Differential B-Cell responses are induced by Mycobacterium tuberculosis Ag85A synthetic peptides in two populations from Venezuela

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Background: The aim of the present study was to assess progress made in the diagnosis of pulmonary tuberculosis when evaluating B-cell responses to 16 Ag85A synthetic peptides, the recombinant antigen 85 (rAg85) and the non-recombinant PPD antigen.

Methods: The B-cell responses of tuberculosis patients and healthy individuals were evaluated by an IgG-ELISA. A total of 120 individuals were included in this study. Patient groups were conformed of 20 Warao indigenous (WP) and 20 Creole non-indigenous (CP), whilst healthy control groups were composed by 40 Warao indigenous (WC) and 40 Creole non-indigenous (CC). Both control groups included 20 positive and 20 negative individuals for the tuberculin skin test (TST). Association of positive tests for each antigen, defined with receiver operator characteristics (ROC) analysis, was assessed for each population.

Results: Different patterns of the B-cell responses were displayed by each population. The anti-29878 IgG method reached highest sensitivity of 95.0% (negative predictive value (NPV) = 94.4) within the Warao population, but was lowly specific, 42.5%, (positive predictive value (PPV) = 45.2), compared to highest specificity showed by the anti-29879 IgG method (100.0%, PPV = 100). Regarding the Creole population, anti-11006 IgG showed highest sensitivity of 95.0% (NPV = 90) but was lowly specific (22.5%, PPV = 38). Anti-10998 IgG was found to be the most specific (100.0%, PPV = 100), followed by the anti-PPD IgG method (90.0%, PPV = 66.7). These findings indicate that population-to-population heterogeneity of peptide antigen recognition, rather than recognition of particular antigens, is a characteristic feature of antibody responses in these two populations. Furthermore, responses to anti-29879 IgG and anti-10998 IgG were associated to inactive TB.

Conclusion: Ag85A peptides were more specific than sensitive, showing that these peptides' high specificity does not stimulate primed T cells in TST+ individuals, suggesting that